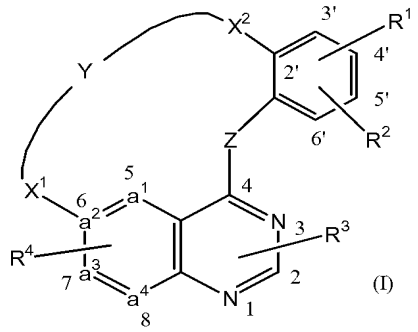
ABSTRACT

PYRIDO- AND PYRIMIDOPYRIMIDINE DERIVATIVES

The present invention concerns the compounds of formula



(I)

the *N*-oxide forms, the pharmaceutically acceptable addition salts and the stereochemically isomeric forms thereof, wherein

a^1-a^2=a^3-a^4 represents a divalent radical selected from N-CH=CH-CH, N-CH=N-CH or CH-CH=N-CH;

Z represents NH; Y represents -C_{3-9}alkyl-, -C_{1-5}alkyl-NR^{13}-C_{1-5}alkyl-, -C_{1-6}alkyl-NH-CO- or -CO-NH -C_{1-6}alkyl- ;

X^1 represents -O- or -NR^{11}-; X^2 represents -C_{1-2}alkyl-, -O-C_{1-2}alkyl, -O- or –O-CH_2-;

R^1 represents hydrogen or halo;

R^2 represents hydrogen, cyano, halo, hydroxycarbonyl-, C_{1-4}alkyloxycarbonyl-, Het^{16}-carbonyl- or Ar^5; R^3 represents hydrogen;

R^4 represents hydroxy, C_{1-4}alkyloxy-, Ar^4-C_{1-4}alkyloxy or R^4 represents C_{1-4}alkyloxy substituted with one or where possible two or more substituents selected from C_{1-4}alkyloxy- or Het^2-;

R^{11} represents hydrogen;

R^{12} represents hydrogen, C_{1-4}alkyl- or C_{1-4}alkyl-oxy-carbonyl-;

R^{13} represents Het^{14}-C_{1-4}alkyl, in particular morpholinyl-C_{1-4}alkyl;

Het^2 represents a heterocycle selected from morpholinyl or piperidinyl optionally substituted with C_{1-4}alkyl-, preferably methyl;

Het^{14} represents morpholinyl;

Het^{16} represents a heterocycle selected from morpholinyl or pyrrolidinyl;

Ar^4 represents phenyl; Ar^5 represents phenyl optionally substituted with cyano.